

ORIGINAL ARTICLES

Campylobacter spp Gastroenteritis in Paediatric Patients of a Portuguese Hospital: Impact of the COVID-19 Pandemic

Gastroenterite por *Campylobacter* spp na População Pediátrica de um Hospital Português: Impacto da Pandemia COVID-19

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ABSTRACT

Introduction: *Campylobacter* spp is the main cause of acute bacterial gastroenteritis. This study aims to characterise cases of *Campylobacter* spp acute gastroenteritis (CAG) over the past 10 years in a Portuguese hospital setting and to assess the impact of the COVID-19 pandemic on the incidence and management of these infections.

Methods Observational descriptive study of CAG in a Portuguese Paediatrics Department, from 01. June.2013 to 31. December.2023. Diagnosis was established by stool culture/molecular methods.

Results: Among 3391 stool samples analysed, 766 tested positive, and *Campylobacter* spp was isolated in 582 of them. A total of 502 CAG were diagnosed: 89% caused by *C. jejuni*, 63% were male, and the median age was 2 years. Co-infections were found in 12% of the cases. The incidence of CAG increased over the years, mainly after the emergence of the COVID-19 pandemic.

Conclusions: Over the last 10 years, there has been an increase of CAG, mainly affecting young children and boys. After COVID-19, the incidence of campylobacteriosis increased, for reasons that remain to be clarified. Although the clinical course was mostly benign, the acute complications raised after the pandemic.

Keywords: *Campylobacter*; COVID-19; epidemiology; gastroenteritis

RESUMO

Introdução: O *Campylobacter* spp é a principal causa de gastroenterite aguda bacteriana. Este estudo tem como objetivo caracterizar os casos de gastroenterite aguda por *Campylobacter* spp (GAC) nos últimos 10 anos num hospital português e avaliar o impacto da pandemia COVID-19 na incidência e abordagem destas infeções.

Métodos: Estudo observacional descritivo de GAC num Serviço de Pediatria português, desde 1.junho.2013 a 31.dezembro.2023. O diagnóstico foi estabelecido por coprocultura/métodos moleculares.

Resultados: De 3391 análises às fezes, 766 foram positivas, e 582 isolaram *Campylobacter* spp. Diagnosticaram-se 502 GAC: 89% *C. jejuni*. A maioria dos casos (62.4%) ocorreu em rapazes, e a idade mediana foi de 2.18 anos. Foram encontradas co-infeções em 12%. A incidência de GAC tem aumentado ao longo dos anos, principalmente depois do aparecimento da COVID-19.

Conclusões: Nos últimos 10 anos tem havido um aumento de GAC, que afeta principalmente crianças pequenas do sexo masculino. Depois da COVID-19, a incidência de campilobacterioses aumentou, por razões que ainda estão por esclarecer. Embora a evolução seja

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maioritariamente benigna, as complicações agudas aumentaram após a pandemia.

Palavras-chave: *Campylobacter*; COVID-19; epidemiologia; gastroenterite

INTRODUCTION

Campylobacter spp is a gram-negative helical bacterium frequently isolated in the faeces of cattle, pigs, birds and some pets, and may also be present in sources of untreated water, unpasteurized milk, contaminated food or undercooked meat. It has not been identified in the intestine of healthy humans, constituting an important intestinal pathogen and nowadays the main cause of acute bacterial gastroenteritis in children in developed countries.⁽¹⁻⁹⁾

Currently, 20 species of *Campylobacter spp* are known. The main ones are *C. jejuni* and *C. coli*, but there are others, such as *C. upsalensis*, *C. lari*, *C. urealyticus* and *C. fetus*, which can also cause infectious disease in humans.⁽¹⁻⁹⁾

After an incubation period of approximately 3 days, *Campylobacter spp* infection cause diarrhoea, often bloody, fever, abdominal pain, anorexia and occasionally nausea and vomiting.^(1,3-5,7,8,11)

The occurrence of extraintestinal complications, acute or late, is relatively low, but not negligible, and may be secondary to bacterial invasion or immune-mediated mechanisms. Bacteraemia, meningitis, osteomyelitis, myocarditis, pericarditis, erythema nodosum, glomerulonephritis, haemolytic anaemia, reactive arthritis and Guillain-Barré syndrome may occur.^(1,4,6,7,11)

The diagnosis is established based on a stool culture (results available in two to three days) or nucleic acid amplification tests (NAAT) in stools using the reverse transcription-polymerase chain reaction (RT-PCR) technique. RT-PCR allowed faster and more sensitive diagnosis, however it is more expensive, it takes longer to test negative and does not enable antimicrobial susceptibility to be assessed. Stool culture continues to be the gold standard for diagnosis.^(1,2,4,6,7,11)

Acute gastroenteritis caused by *Campylobacter spp* is usually mild and self-limited. The focus of treatment is adequate hydration and correction of electrolyte imbalances, with antibiotics reserved for severe or potentially severe cases.^(1,3,4,7)

In the last two decades, an increase in the incidence of *Campylobacter spp* infection has been reported in several parts of the world, including Europe, the United States of America and Israel.^(2,4,7)

The purpose of this study was to characterize the acute gastroenteritis caused by *Campylobacter spp* over the last 10 years, and to evaluate the impact of the COVID-19 pandemic on the infection.

MATERIALS AND METHODS

Observational descriptive study of *Campylobacter spp* infections in the Paediatrics Department (emergency, outpatient, and inpatient settings) of a level I hospital in Portugal, from 01 June 2013 to 31 December 2023.

Diagnosis was established based on the *Campylobacter's* identification by stool culture (selective medium for isolation of intestinal *Campylobacter*, Biomériuex® Campyloesel Agar) and/or molecular methods (QIAstat-Dx® Gastrointestinal Panel). Access to all stool tests carried out in the Microbiology Department was available: culture data since June 2013, and RT-PCR multiplex gastrointestinal panel available since June 2020. Children and adolescents under 18 years of age with at least one positive laboratory test for *Campylobacter spp* were included in the analysis.

Data on sex, age, co-infections, acute complications, symptoms, antibiotic treatment and antimicrobial susceptibility were collected from medical records.

RESULTS

During the study period, a total of 3391 stool analyses (culture and NAAT) were performed. Of these, 766 tested positive for at least one microorganism and 582 were positive for *Campylobacter spp*. *Campylobacter spp* was the leading bacterial cause of infection identified each year, accounting for 502 cases (Table 1).

The annual distribution of infections (Figure 1) shows a progressive increase over the years, more pronounced from 2020 onwards – the first year of the COVID-19 pandemic. The annual incidence of the infection confirms this increment after the emergence of COVID-19.

Monthly distribution of infections did not show a clear seasonal pattern over the study period (Figure 2).

Of the 502 *Campylobacter spp* infections, 62.4% occurred in males (n=313) and the median age of the children was 2.18 years (minimum; maximum 17 years).

The main species isolated was *Campylobacter jejuni* in 89.2% of the cases (n=448), followed by *C. coli* (n=26), *C. upsalensis* (n=22), *C. fetus* (n=2), *C. lari* (n=1). In 3 cases, the species was not identified as the infection was only diagnosed through the NAAT.

Gastrointestinal co-infection was identified in 11.3% (n=57), mainly with rotavirus and adenovirus (n=52). Other co-infecting agents included enteropathogenic *E.coli* (n=1), *Yersenia enterocolitica* (n=1),

E.coli prod Shiga stx1/stx2 (n=1), enterovirus (n=1) and sapovirus (n=1).

Clinically, the most common symptoms were diarrhoea (99.6%), blood in the stool (68.9%) and fever (66.7%). Almost half of the patients had mucus in the stool (49%), anorexia (42.8%), abdominal pain (38%) and vomiting (31.1%).

Antibiotics were prescribed in 20.9% of the cases (n=105, 75 with macrolide). Antimicrobial susceptibility testing is no longer routinely performed at hospital. However, it was conducted in 138 cases, of which 116 were sensitive and 12 (8.7%) were resistant to

erythromycin.

There were six cases (1.2%) of acute complications, all of which followed the onset of COVID-19 pandemic, two of them had gastrointestinal co-infection: three cases of nephritic syndromes; one case of sepsis with meningitis, one case of hypovolemic and septic shock (*C. jejuni* and *E.coli enteropathogenic*) and one case of acute myocarditis with cardiogenic shock (*C. jejuni* and enterovirus). Except for one boy with nephritic syndrome who had a history of *Henoch-Schönlein* purpura few months before, all the other children were previously healthy.

Table 1 - Annual distribution of stool analyses (cultures and RT-PCR multiplex panels) performed, positive for any microorganism and positive for *Campylobacter spp.*

		2013 (jun-dec)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	Total
No of analyses performed	cultures	148	245	207	261	303	353	344	252	299	446	496	3391
	RT-PCR	0	0	0	0	0	0	0	6	2	3	26	
No of positive analyses	cultures	18	26	43	50	51	53	71	89	93	119	129	766
	RT-PCR	0	0	0	0	0	0	0	3	1	1	19	
No of positive analyses for <i>Campylobacter spp</i>	cultures	11	16	23	37	42	45	55	69	82	92	103	582
	RT-PCR	0	0	0	0	0	0	0	1	0	0	6	

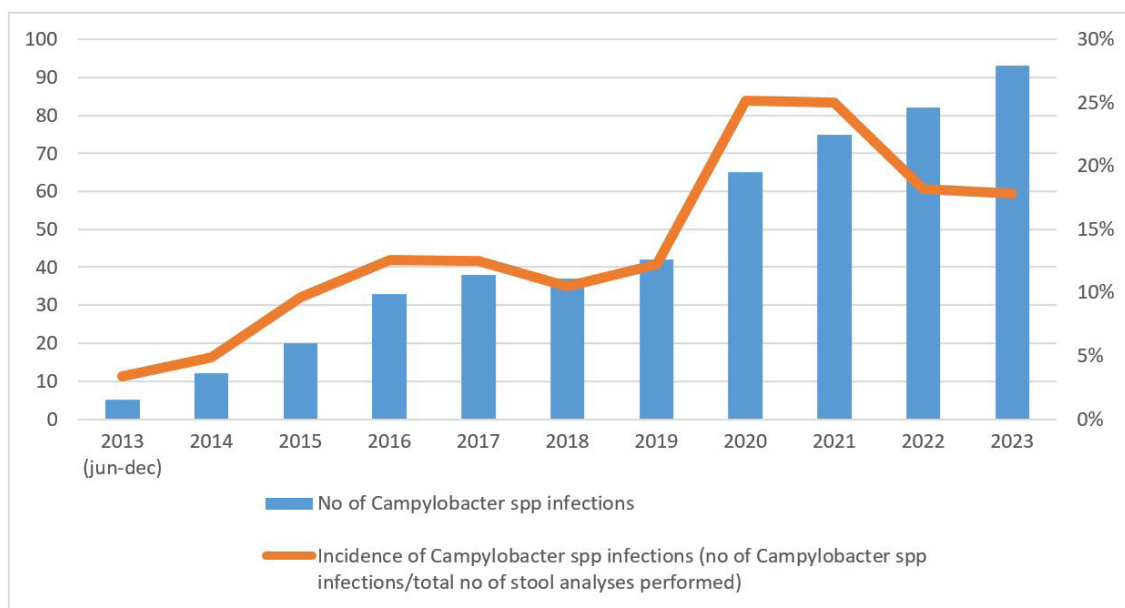


Figure 1 – Annual distribution of *Campylobacter spp* infections and its incidence

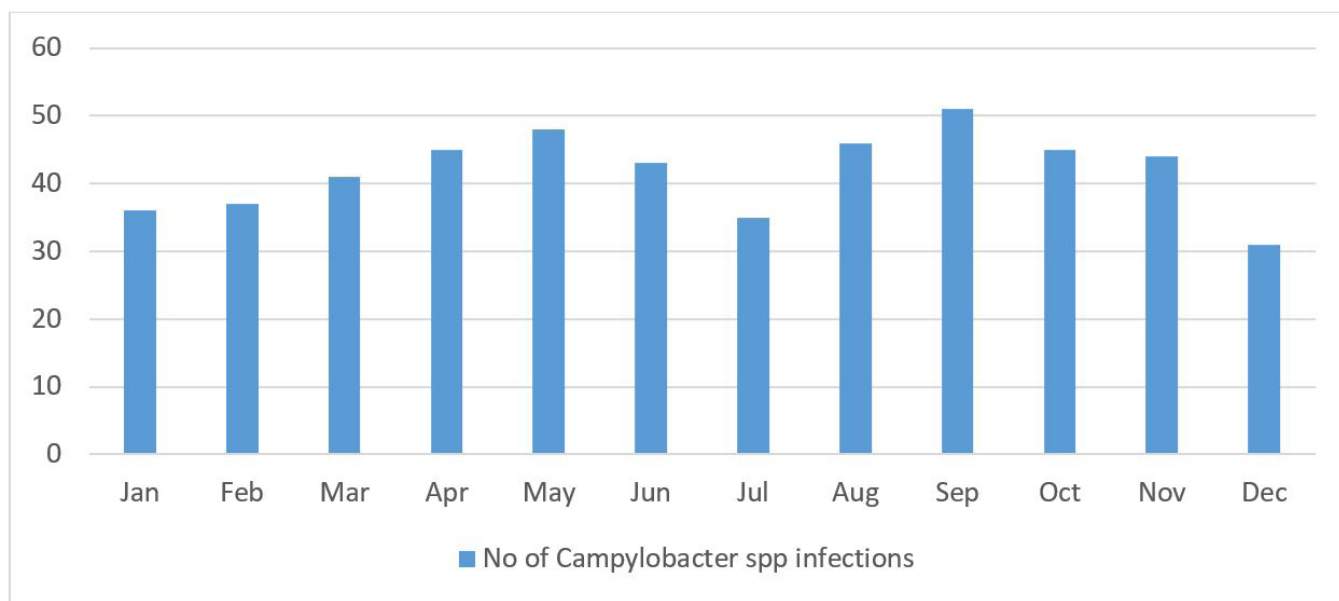


Figure 2 – Monthly distribution of *Campylobacter spp* infections

DISCUSSION

Over the last ten years, a progressive increase of the identification of *Campylobacter spp* in stools has been observed. The incidence of the infection was noticeably more marked after 2020, the first year of the COVID-19 pandemic. Although efforts to control the transmission of other infectious agents during the pandemic have been effective in reducing the incidence of several transmitted diseases, the number of campylobacteriosis has increased compared to previous years. In Luxembourg, France, Lithuania and Latvia there was also an increase in 2020 compared to the average incidence reported in pre-pandemic years.⁽⁸⁾ The reasons behind this rise are still unknown, and so far no new strains or changes in the bacteria's virulence mechanism allowing a greater transmission have been described. Certainly the new molecular biology tests have increased the sensitivity of diagnosis compared to classic stool cultures. Despite being introduced in our hospital in June 2020, we only had three *Campylobacter spp* infections that were diagnosed by RT-PCR without isolation in stool culture. There were probably some individual variability in the analysis' request at our hospital, because the criteria to perform stool cultures and multiplex faecal panel are not protocolled. However, this does not seem to have a great influence on the results found since there are general orientations to perform stool analyses in cases of acute gastroenteritis with prolonged diarrhoea (>7 days), bloody diarrhoea, high fever, severe abdominal pain, underlying chronic diseases (inflammatory bowel disease, immunodeficiencies, oncological diseases, malnutrition, etc.) and history of recent travel to risk areas or outbreaks.^(3,11) As reported in the literature, gastrointestinal infection by *Campylobacter spp* was

more common in males and mainly affected young children (median age of 2.18 years).^(3,5,12) This last finding could be explained by the high infection's transmission rate in young children, especially those who still wear diapers, and by the fact that primary infections tend to be more severe and therefore tested more frequently.⁽²⁾ In contrast to the usual summer peak incidence described in some studies, we did not see a clear seasonality over the years. The main species identified was undoubtedly *C. jejuni*, followed by *C. coli* and *C. upsalensis*, but we also had three cases of gastrointestinal infection by *C. lari* and *C. fetus*.^(2,3,5,6)

Clinically, diarrhoea was present in almost all cases and vomiting was the least frequent symptom, as it is more associated with viral infections.⁽¹¹⁾ Antibiotics should always be restricted for the most serious or potentially serious infections and the first-line option should be azithromycin (at a dose of 10mg/kg/day for a maximum of 500mg/day for three days).^(1,3-5) The rate of resistance to macrolides remains low, in our study it was <10%, despite the limited sample tested for antimicrobial susceptibility.^(1,5,7,13)

Although the evolution was mostly benign, acute complications increased after the onset of the COVID-19 pandemic. Nephritic syndrome is not one of the most commonly described complications in the literature, but it was the most frequent in our sample (n=3). Some cases have been reported showing a potential relationship between this infection and the development of glomerular disease through immune mechanisms.⁽⁹⁾ There has also been an increase of reported cases of myocarditis and pericarditis associated with *Campylobacter spp*.^(7,9) Bacteraemia tends to occur in 0.1 to 1% of cases, being more common in immunocompromised patients.⁽¹⁾

In conclusion, campylobacteriosis have been increasingly identified in recent years, especially after the start of the COVID-19 pandemic.

The reasons for this fact remain to be clarified, although the role of new molecular tests may have an influence.

AUTHORSHIP

Joana De Beir - Analysis and interpretation of data; drafting the manuscript and revising it critically for important intellectual content; final approval of the version to be published

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Silvia Almeida - Conception and design of the study; drafting the manuscript and revising it critically for important intellectual content; final approval of the version to be published

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